REMARKS

Claims 20 and 24-26 are pending in the subject application. By this amendment, applicants have amended claims 20 and 24 in order to better clarify the subject invention. Applicants maintain that the amendments to the claims do not raise an issue of new matter. Support for the amendments to claim 20 can be found at least in the previous version of the claim. Support for the amendments to claim 24 can be found *inter alia* in the specification at least on page 8, lines 12-15, and page 10, lines 19-22. Accordingly, applicants respectfully request that the Amendment be entered.

Rejection of Claim 20 under 35 U.S.C. §103(a)

Claim 20 stands rejected under 35 U.S.C. §103(a) as unpatentable over Olsson et al., 1983, J. Appl. Biochem. 5:437-445.

Applicants respectfully traverse this rejection for the following reasons. Applicants maintain that Olsson does not does not suggest the claimed method for diagnosing erythrocyte hemolysis in a subject wherein "the presence of at least about 20 U/L erythrocyte adenylate kinase activity in ... [a serum sample obtained from the subject is] indicative of erythrocyte hemolysis in said subject."

Applicants note that the Examiner has previously pointed out that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re* Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Applicants request that the Examiner give further consideration to the following.

Applicants note that Table 1 in the subject application clearly indicates that low levels of adenylate kinase activity can be present in the absence of hemoglobin, and that there is thus a threshold for erythrocyte adenylate kinase activity, above which erythrocyte adenylate kinase activity is indicative of erythrocyte hemolysis. Applicants

maintain that Olsson does not suggest the need to determine a threshold level of erythrocyte adenylate kinase activity, above which values of erythrocyte adenylate kinase activity are indicative of erythrocyte hemolysis. In contrast, Figure 6 of Olsson indicates that there is no threshold and thus teaches away from the claimed invention. The claimed invention thus achieves an unexpected result relative to the teachings of Olsson, namely the present invention sets forth, as part of the claimed method for diagnosing erythrocyte hemolysis in a subject, an erythrocyte adenylate kinase activity threshold that is not obvious from the teachings of Olsson (i.e., contrast Figure 6 in Olsson).

Applicants maintain that the "general conditions" of the subject invention as a whole, as discussed in *In re* Aller (*supra*), are not set forth in Olsson because Olsson does not set forth the concept of a threshold for erythrocyte adenylate kinase activity as part of a method for diagnosing erythrocyte hemolysis in a subject. Applicants further note that the court in *In re* Aller further stated that changes such as a change in temperature, or in concentration, or in both, "may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art." *In re* Aller, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Applicants maintain that the subject invention is not a mere optimization of Olsson, but rather that the erythrocyte adenylate kinase activity threshold set forth in the subject invention is an unexpected result that is both different in kind and not obvious from the teachings of Olsson.

Applicants further note that the court in *In re* Antonie stated:

> In *In re* Aller, 42 CCPA 824, 220 F.2d 454, 105 USPQ 233 (1955), the court set out the rule that the discovery of an optimum value of a variable in a known process is normally obvious. We have found exceptions to this rule in cases where the results of optimizing a variable, which was known to be result effective, were unexpectedly good. [citations omitted] This case, in which the parameter optimized was not recognized to be a result-effective variable, is another exception. *In re* Antonie, 559 F.2d 618,

620, 195 USPQ 6, 8-9 (CCPA 1977).

Applicants maintain that Olsson did not suggest the need to determine, let alone optimize, erythrocyte adenylate kinase activity threshold and therefore erythrocyte adenylate kinase activity threshold was not recognized in the art to be a "result-effective variable" in a method for diagnosing erythrocyte hemolysis in a subject. Thus, the present case falls within the exception recognized in *In re* Antonie to the general rule set forth in *In re* Aller.

In view of the reasons set forth herein above, applicants maintain that Olsson does not suggest the claimed invention and thus that Olsson does not render the claimed invention obvious. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Rejection of Claims 24-26 under 35 U.S.C. §103(a)

Claims 24-26 are rejected under 35 U.S.C. §103(a) as unpatentable over Olsson et al., 1983, J. Appl. Biochem. 5:437-445, as applied to claim 20, and further in view of Matsura et al., 1989, J. Appl. Biochem. 264:10148-55.

Applicants respectfully traverse this rejection. Applicants maintain that claim 20 is patentable over Olsson for the reasons set forth herein above. Claims 24-26 depend from, and further limit, claim 20. Accordingly, applicants maintain that claims 24-26 are patentable over the cited references, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

CONCLUSIONS

In view of the remarks made herein above, reconsideration and withdrawal of the rejections in the August 22, 2003 Final Office Action are respectfully requested. If there are any minor matters that would prevent allowance of the subject application, the Patent Office is requested to telephone the undersigned attorney.

No fee is deemed necessary in connection with the submission of this response. However, if any fee is required to maintain the pendency of the subject application, the Patent Office is authorized to withdraw the amount of any such fee from Deposit Account No. 01-1785.

Respectfully submitted,

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